118

What is claimed is:

1. A compound of the Formula (I)

wherein

5

15

20

R is a linking moiety;

10 R¹ is selected from the group consisting of H, C₁ -C₆ alkyl and acyl;

M is selected from the group consisting of O, S, NH, NR⁴, NOH and NOR⁴;

R² is selected from the group consisting of H, halogen, alkyl, alkenyl, alkynyl, haloalkenyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, heteroaryloxy, arylalkyloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, phenoxy, benzyloxy, COOR4, CONHR4, NHCOR4, NHCOOR⁴, NHCONHR⁴, C(=NOH)R⁴, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, aminosulfinyl, SR4 and acyl; each of which may optionally be substituted,

25 or

R² together with the nitrogen to which it is attached and a portion of R form an optionally substituted heterocycloalky group;

R³ is selected from the group consisting of H, halogen, alkyl, alkenyl, alkynyl, alkenyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkenyl, heterocycloalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy,



heteroaryloxy, arylalkyloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, phenoxy, benzyloxy, COOR⁴, CONHR⁴, NHCOR⁴, NHCOOR⁴, NHCONHR⁴, C(=NOH)R⁴, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, arylsulfonyl, arylsulfonyl, aminosulfonyl, aminosulfonyl, SR⁴ and acyl; each of which may optionally be substituted;

Q is selected from the group consisting of $-S(O)_{2-}$, -C(=O)- and -C(=S)-;

G is selected from the group consisting of optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted arylalkyl, and optionally substituted heteroarylalkyl;

each R⁴ is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl, each of which may be optionally substituted;

or a pharmaceutically acceptable salt or prodrug thereof.

20

25

30

15

5

2. A compound according to claim 1 having the Formula (2)

wherein

R¹ is selected from the group consisting of H, C₁ -C₆ alkyl and acyl;

L is a single bond or is a C_1 - C_5 hydrocarbon chain which may contain 0 to 2 multiple bonds independently selected from double bonds and triple bonds and wherein, the chain may optionally be interrupted by at least one of -O-, -S-, -S(O)- and -S(O)₂- and the chain may optionally be substituted with one or more substituents independently selected from the group consisting of C_1 - C_4 alkyl;

120

Z is selected from the group consisting of a single bond, N(R1), O, S, S(O) and S(O)2;

A is selected from the group consisting of a single bond, optionally substituted arylene, optionally substituted heteroarylene, optionally substituted cycloalkylene and optionally substituted heterocycloalkylene;

B is selected from the group consisting of a single bond, optionally substituted aminoacyl, optionally substituted arylene, optionally substituted heteroarylene, optionally substituted arylalkylene, optionally substituted heteroarylalkylene, optionally substituted alkylarylene, optionally substituted alkylheteroarylene, optionally substituted C1-C3 alkylene, optionally substituted heteroalkylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene and optionally substituted -(CH₂)_m-C(O)-N(R⁴)- $(CH_2)_{n-1}$, wherein n is an integer from 0 to 6, m is an integer from 0 to 6;

15

20

25

30

35.

10

5

M is selected from the group consisting of O, S, NH, NR⁴, NOH and NOR⁴:

R² is selected from the group consisting of H, halogen, alkyl, alkenyl, alkynyl, haloalkenyl, heteroalkyl, haloalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl. heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl. heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, heteroaryloxy, arylalkyloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, phenoxy, benzyloxy, COOR⁴, CONHR₄, NHCOR⁴, NHCOOR⁴ NHCONHR⁴, C(=NOH)R⁴, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, aminosulfinyl, SR4 and acyl; each of which may optionally be substituted, or

R² together with the nitrogen to which it is attached and a portion of B form an optionally substituted heterocycloalky group;

R³ is independently selected from the group consisting of H, halogen, alkyl, alkenvl. alkynyl, haloalkyl, haloalkenvi. heteroalkyl, cycloalkyl, cycloalkenyl. heterocycloalkyl, heterocycloalkenyl, aryl. heteroaryl. cycloaikylaikyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl,

121

alkoxy, alkoxyalkyl, alkoxyaryi, alkenyloxy, alkynyloxy, cycloalkylkoxy. heterocycloalkyloxy, aryloxy, heteroaryloxy, arylalkyloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, phenoxy, benzyloxy, COOR4, CONHR⁴, NHCOR⁴, NHCOOR4. NHCONHR⁴, C(=NOH)R4, alkoxycarbonyl. alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, aminosulfinyl, SR4 and acyl; each of which may optionally be substituted;

Q is selected from the group consisting of $-S(O)_{2^{-}}$, -C(=O)- and -C(=S)-;

G is selected from the group consisting of optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl;

each R⁴ is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl; each of which may be optionally substituted;

or a pharmaceutically acceptable salt or prodrug thereof.

3. A compound according to claim 1 or 2 having the Formula (2a)

wherein

25

R1 is selected from the group consisting of H, C1 -C8 alkyl and acyl;

L is a single bond or is a C₁-C₅ hydrocarbon chain which may contain 0 to 2 multiple bonds independently selected from double bonds and triple bonds and wherein, the chain may optionally be interrupted by at least one of -O-, -S-, -S(O)- and -S(O)₂- and

the chain may optionally be substituted with one or more substituents independently selected from the group consisting of C₁-C₄ alkyl;

Z is selected from the group consisting of a single bond, $N(R^1)$, O, S, S(O) and $S(O)_2$;

A is selected from the group consisting of a single bond, optionally substituted arylene, optionally substituted heteroarylene, optionally substituted cycloalkylene and optionally substituted heterocycloalkylene;

10

15

B is selected from the group consisting of a single bond, optionally substituted aminoacyl, optionally substituted arylene, optionally substituted heteroarylene, optionally substituted arylalkylene, optionally substituted heteroarylene, optionally substituted alkylarylene, optionally substituted alkylheteroarylene, optionally substituted C_1 - C_3 alkylene, optionally substituted heteroalkylene, optionally substituted cycloalkylene optionally substituted heterocycloalkylene and optionally substituted -(CH₂)_m-C(O)-N(R⁴)-(CH₂)_n-, wherein n is an integer from 0 to 6, m is an integer from 0 to 6;

M is selected from the group consisting of O, S, NH, NR⁴, NOH and NOR⁴;

20

25

30

 R^2 is selected from the group consisting of H, C_1 - C_{10} alkyl, alkenyl, heteroalkyl, haloalkyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, C_4 - C_9 heterocycloalkylalkyl, cycloalkylalkyl (e.g., cyclopropylmethyl), arylalkyl (e.g. benzyl), heteroarylalkyl (e.g. pyridylmethyl), hydroxyl, hydroxyalkyl, alkoxy, amino, alkylamino, aminoalkyl, acylamino, phenoxy, alkoxyalkyl, benzyloxy, alkylosulfonyl, arylsulfonyl, aminosulfonyl, - $C(O)OR^4$, - $CONHR^4$, - $NHCONHR^4$, $C(=NOH)R^4$, and acyl;

 R^3 is selected from the group consisting of H, C_1 - C_{10} alkyl, alkenyl, heteroalkyl, haloalkyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, C_4 - C_9 heterocycloalkylalkyl, cycloalkylalkyl (e.g., cyclopropylmethyl), arylalkyl (e.g. benzyl), heteroarylalkyl (e.g. pyridylmethyl), hydroxyl, hydroxyalkyl, alkoxy, amino, alkylamino, aminoalkyl, acylamino, phenoxy, alkoxyalkyl, benzyloxy, alkylosulfonyl, arylsulfonyl, aminosulfonyl, - $C(O)OR^4$, - $CONHR^4$, - $NHCONHR^4$, $C(=NOH)R^4$, and acyl;

123

G is selected from optionally substituted aryl, optionally substituted heteroaryl, alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted heterocycloalkyl, optionally substituted arylalkyl and optionally substituted heterocycloalkyl, wherein the substituents are independently selected from the group consisting of X, Y, R⁴, hydroxyl, hydroxyalkyl, alkoxy, amino, alkylamino, aminoalkyl, acylamino, phenoxy, alkoxyalkyl, benzyloxy, alkylosulfonyl, arylsulfonyl, aminosulfonyl, -C(O)OR⁴, -C(O)OH, -SH, -CONHR⁴, -NHCONHR⁴, and C(=NOH)R⁴;

R⁴ is selected from the group consisting of C₁-C₄ alkyl, heteroalkyl, aryl, heteroaryl and acyl;

X and Y are the same or different and are independently selected from the group consisting of H, halo, C₁-C₄ alkyl, NO₂, OR⁴, SR⁴, C(O)R⁵, and NR⁶R⁷;

15 R⁵ is C₁-C₄ alkyl;

 R^6 and R^7 are the same or different and are independently selected from the group consisting of H, C_1 - C_6 alkyl, C_4 - C_9 cycloalkyl, C_4 - C_9 heterocycloalkyl, aryl, heteroaryl, arylalkyl and heteroaryl alkyl.

or a pharmaceutically acceptable salt or prodrug thereof.

4. A compound according to claim 2 or 3 having the Formula (2b)

$$G \longrightarrow Q \longrightarrow N \longrightarrow M$$

$$\downarrow N \longrightarrow B \longrightarrow A \longrightarrow L$$

$$\downarrow N \longrightarrow D$$

Formula (2b)

or a pharmaceutically acceptable salt or prodrug thereof.

5. A compound according to any one of claims 2-4 having the Formula (2c)

25

or a pharmaceutically acceptable salt or prodrug thereof.

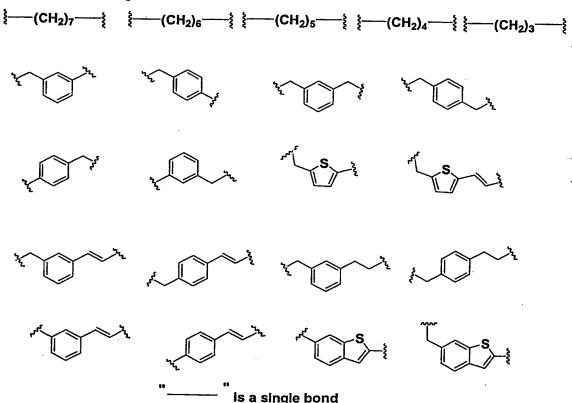
10

15

- 5 6. A compound according to any one of claims 2 to 4 wherein A is optionally substituted arylene.
 - 7. A compound according to any one of claims 2 to 4 wherein A selected from the group consisting of 1,4-phenylene and 1,3-phenylene.
 - 8. A compound according to any one of claims 2 to 4 wherein A is 1,4-phenylene.
 - 9. A compound according to any one of 2 to 8 wherein L is selected from the group consisting of a single bond, $-CH_2$ -, $-(CH_2)_2$ and -CH=CH-.
 - 10. A compound according to any one of claims 2 to 9 wherein L is a bond.
 - 11. A compound according to any one of claims 2 to 9 wherein L is a group of formula -CH₂-.
 - 12. A compound according to any one of claims 2 to 9 wherein L is a group of formula –CH=CH-.
- 13. A compound according to any one of claims 2 to 12 wherein B is selected from the
 25 group consisting of a single bond, methylene, ethylene, propylene, alkylarylene, and heteroalkylene.
 - 14. A compound according to any one of claims 2 to 13 wherein B is methylene.
- 30 15. A compound according to any one of claims 2 to 13 wherein B is a single bond.
 - 16. A compound according to any one of claims 2 to 13 wherein B is ethylene.

125

- 17. A compound according to any one of claims 2 to 13 wherein B is propylene.
- 18. A compound according to claim 2 or 3 wherein the group BAZL is a group of formula $-(CH_2)_{n}$ wherein n is an integer from 1 to 7.
- 19. A compound according to claim 2 or 3 wherein the group BAZ is a group of formula $-(CH_2)$ phenyl-.
- 20. A compound according to claim 2 or 3 wherein the group BAZL is selected from the group consisting of



- 21. A compound according to any one of claims 2 to 20 wherein R² and a portion of B together with the nitrogen to which they are attached form a heterocyloalkylene.
- 22. A compound according to claim 21 wherein the heterocycloalkylene is 1,4-piperazinylene.
- 23. A compound according to any one of claims 1 to 22 wherein $R^1 = H$.

20

126

- 24. A compound according to any one of claims 1 to 23 wherein M is O.
- 25. A compound according to any one of claims 1 to 23 wherein M is S.
- 5 26. A compound according to any one of claims 1 to 23 wherein Q is S(O)₂.
 - 27. A compound according to any one of claims 1 to 23 wherein Q is CO.
- 28. A compound according to any one of claims 1 to 27 wherein G is optionally substituted aryl.
 - 29. A compound according to any one of claims 1 to 28 wherein G is phenyl.

15

- 30. A compound according to any one of claims 1 to 28 wherein G is 4-methylphenyl.
- 31. A compound according to any one of claims 1 to 30 wherein R² is selected from the group consisting of H, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted arylalkyl, optionally substituted arylalkyl, optionally substituted arylalkyl, optionally substituted heteroarylalkyl, optionally substituted heteroarylalkyl, optionally substituted heteroarylalkyl, optionally substituted heteroarylalkyl, optionally substituted heterocycloalkylalkyl.
- 32. A compound according to any one of claims 1 to 31 wherein R² is selected from 25 the group consisting of H, 2-(1H-indol-3-yl)-ethyl, 2-(2-methyl-1H-indol-3-yl)-ethyl, pyridin-3-ylmethyl, 3-hydroxy-propyl, 2-pyridin-2-yl-ethyl, 2-pyridin-3-yl-ethyl, pyridin-3-ylmethyl, 2-pyridin-4-yl-ethyl, benzyl, 3-phenyl-propyl, 2-phenoxy-ethyl, morpholin-4-yl, pyridin-2-yl, phenethyl, 2-(4-bromo-phenyl)-ethyl, 2-(4-fluoro-phenyl)-ethyl, 3-imidazol-1-yl-propyl, 2-(1H-imidazol-4-yl)-ethyl, 1H-Benzoimidazol-2-ylmethyl, 2-piperidin-1-yl-ethyl, 2-pyrrolidin-30 1-yl-ethyl, 2-cyclohex-1-enyl-ethyl, 2-ethyl-hexyl, 2-thiophen-2-yl-ethyl, 3,3-diphenylpropyl, 2-biphenyl-4-yl-ethyl, -(4-phenoxy-phenyl, 2-(3-phenoxy-phenyl)-ethyl, 2-(2.3dimethoxy-phenyl, 2-(2,4-dichloro-phenyl)-ethyl, cyclohexylmethyl, hexyl, isobutyl, 3isopropoxy-propyl, 2-phenoxy-ethyl, 2-isopropoxy-ethyl, 3-methoxy-benzyl, 4-[1,2,3]thiadiazol-4-yl-benzyl, 2,4-dichloro-benzyl, 2-(2-methoxy-phenyl)-ethyl, 2-(3-fluoro-35 phenyl)-ethyl, 2-(2-fluoro-phenyl)-ethyl, 2,2-diphenyl-ethyl, 2-(4-methoxy-phenyl)-ethyl, 2-(3-chloro-phenyl)-ethyl, 4-phenyl-butyl, 3-phenyl-propyl, 3,3-diphenyl-propyl, 3-(4-methylpiperazin-1-yl, 3-morpholin-4-yl-propyl, 3-(2-oxo-pyrrolidin-1-yl)-propyl, 3-pyrrolidin-1-yl-

127

propyl, tetrahydro-furan-2-ylmethyl, 1,5-dimethyl-hexyl, 2-diethylamino-ethyl and 2-dimethylamino-ethyl.

- 33. A compound according to any one of claims 1 to 31 wherein R² is selected from the group consisting of H, 2-(1H-indol-3-yl)-ethyl, 2-(2-methyl-1H-indol-3-yl)-ethyl, pyridin-3-ylmethyl, 3-hydroxy-propyl, 2-pyridin-2-yl-ethyl, 2-pyridin-3-yl-ethyl, pyridin-2-ylmethyl, pyridin-3-ylmethyl, 2-pyridin-4-yl-ethyl, benzyl, 3-phenyl-propyl, 2-phenoxy-ethyl, 2-morpholino ethyl, 2-phenyl ethyl, 2-(4-bromo-phenyl)-ethyl, 2-(4-fluoro-phenyl)-ethyl, 3-imidazol-1-yl-propyl, 2-(1H-imidazol-4-yl)-ethyl, 1H-Benzoimidazol-2-ylmethyl, 2-piperidin-1-yl-ethyl and 2-pyrrolidin-1-yl-ethyl.
- 34. A compound according to any one of claims 1 to 31 wherein R² is selected from the group consisting of H, 2-(1H-indol-3-yl)-ethyl, 2-(2-methyl-1H-indol-3-yl)-ethyl, 2-phenyl ethyl, 2-piperidin-1-yl-ethyl and 2-pyrrolidin-1-yl-ethyl.

15

20

25

30

10

5

A compound according to any one of claims 1 to 34 wherein the optional 35. substituents are selected from the group consisting of halogen, =O, =S, -CN, -NO2, -CF3, -OCF₃, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalylalkyl, heterocycloalkylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkenyl, heterocycloalkylalkenyl, arylalkenyl, heteroarylalkenyl. cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, arylheteroalkyl, heteroarylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxycycloalkyl, alkoxyheterocycloalkyl, alkoxyaryl, alkoxyheteroaryl, alkoxycarbonyl, alkylaminocarbonyl, alkenyloxy, alkynyloxy, cycloalkyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, phenoxy, benzyloxy, heteroaryloxy, arylalkyloxy, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyloxy, amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonylamino, sulfinylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, sulfinyl, alkylsulfinyl, arylsulfinyl, aminosulfinylaminoalkyl, -COOH, -COR5, -C(O)OR5, CONHR5, NHCOR5, NHCOOR5, NHCONHR⁵, C(=NOH)R⁵, -SH, -SR⁵, -OR⁵ and acyl, wherein each R⁵ is independently selected from the group consisting of alkyl, alkenyl,

alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl, each of which may be optionally substituted;

35

36. A compound according to claim 1 selected from the group consisting of

8-[3-(4-methylbenzenesulfonyl)-ureido])-octanoic acid hydroxyamide,

7-[3-(4-methylbenzenesulfonyl)-ureido])-heptanoic acid hydroxyamide,

6-[3-(4-methylbenzenesulfonyl)-ureido])-hexanoic acid hydroxyamide,

6-[3-(benzenesulfonyl)-ureido])-hexanoic acid hydroxyamide,

N-Hydroxy-4-[3-(4-methylbenzenesulfonyl)ureido]methylbenzamide,

N-Hydroxy-2-{4-[3-(4-methylbenzenesulfonyl)ureido]-phenyl}-acetamide,

N-Hydroxy-2-{3-[3-(4-methylbenzenesulfonyl)ureido]-phenyl}-acetamide,

N-Hydroxy-3-{4-[3-(4-methylbenzenesulfonyl)ureido]-phenyl}-acrylamide,

N-Hydroxy-3-{3-[3-(4-methylbenzenesulfonyl)ureido]-phenyl}-acrylamide,

6-(3-Benzoyl-ureido)-hexanoic acid hydroxyamide,

7-(3-Benzoyl-ureido)-heptanoic acid hydroxyamide,

8-(3-Benzoyl-ureido)-octanoic acid hydroxyamide,

6-[3-Benzoyl-1-(3-phenyl-propyl)-ureido]-hexanoic acid hydroxyamide,

4-(3-Benzoyl-ureidomethyl)-N-hydroxybenzamide,

2-[4-(3-Benzoyl-ureido)-phenyi]-N-hydroxy-acetamide,

2-[3-(3-Benzoyl-ureido)-phenyl]-N-hydroxy-acetamide,

3-[4-(3-Benzoyl-ureido)-phenyl]-N-hydroxy-acrylamide,

3-(4-{3-Benzoyl-1-[2-(1H-indol-3-yl)-ethyl]-ureidomethyl}-phenyl)-N-hydroxyacrylamide,

3-[4-(3-Benzoyl-1-pyridin-3-ylmethyl-ureidomethyl)-phenyl]-N-hydroxy-acrylamide,

3-{4-[3-Benzoyl-1-(3-hydroxy-propyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

4-{3-Benzoyl-1-[2-(1H-indol-3-yl)-ethyl]-ureidomethyl}-N-hydroxy-benzamide,

4-(3-Benzoyl-ureido)-N-hydroxybutyramide,

4-(3-Benzoyl-1-benzyl-ureidomethyl)-N-hydroxy-benzamide,

4-[3-Benzoyl-1-(2-pyridin-2-yl-ethyl)-ureidomethyl]-N-hydroxy-benzamide,

4-[3-Benzoyl-1-(3-hydroxy-propyl)-ureidomethyl]-N-hydroxy-benzamide,

3-[4-(3-Benzoyl-1-benzyl-ureidomethyl)-phenyl]-N-hydroxy-acrylamide,

3-{4-[3-Benzoyl-1-(3-phenyl-propyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

3-{4-[3-Benzoyl-1-(2-phenoxy-ethyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

4-[3-Benzoyl-1-(3-phenyl-propyl)-ureidomethyl]-N-hydroxy-benzamide,

4-(3-Benzoyl-1-pyridin-3-ylmethyl-ureidomethyl)-N-hydroxy-benzamide,

(S)-6-[2-(3-Benzoyl-ureido)-3-(1H-indol-3-yl)-propionylamino]-hexanoic acid hydroxyamide,

4-(4-Benzoylaminocarbonyl-piperazin-1-ylmethyl)-N-hydroxy-benzamide,

7-(3-Benzoyl-1-pyridin-2-ylmethylureldo)-heptanoic acid hydroxyamide,

NH-OH

132

6-(3-Benzoyl-1-pyridin-2-ylmethyl-ureido)-hexanoic acid hydroxyamide,

3-{4-[3-Benzoyl-1-(2-morpholin-4-yl-ethyl)-ureidomethyl]-phenyl}-N-hydroxyacrylamide,

7-(3-Benzoyl-1-benzyl-ureido)-heptanoic acid hydroxyamide,

6-(3-Benzoyl-1-benzyl-ureido)-hexanoic acid hydroxyamide,

3-{4-[3-Benzoyl-1-(2-pyridin-2-yl-ethyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

3-[4-(3-Benzoyl-1-phenethylureidomethyl)-phenyl]-N-hydroxyacrylamide,

3-(4-{3-Benzoyl-1-[2-(4-bromo-phenyl)-ethyl]-ureidomethyl}-phenyl)-N-hydroxy-acrylamide,

3-(4-{3-Benzoyl-1-[2-(4-fluoro-phenyl)-ethyl]-ureidomethyl}-phenyl)-N-hydroxy-

NH HO NH

N-{4-[4-(2-Hydroxycarbamoyl-vinyl)-benzyl]-piperazine-1-carbonyl}-benzamide,

acrylamide,

HO NH NH NH

3-{4-[3-Benzoyl-1-(3-imidazol-1-yl-propyl)-ureidomethyl]-phenyl}-N-hydroxyacrylamide,

N NH NH OH

3-(4-{3-Benzoyl-1-[2-(1H-imidazol-4-yl)-ethyl]-ureidomethyl}-phenyl)-N-hydroxyacrylamide,

6-(3-Benzoyl-thioureido)-hexanoic acid hydroxyamide,

3-{4-[1-(1H-Benzoimidazol-2-ylmethyl)-3-benzoyl-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

3-{4-[3-Benzoyl-1-(2-pyridin-3-yl-ethyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

3-{4-[3-Benzoyl-1-(2-pyridin-4-yl-ethyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

3-{4-[3-Benzoyl-1-(2-piperidin-1-yl-ethyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

3-{4-[3-Benzoyl-1-(2-pyrrolidin-1-yl-ethyl)-ureidomethyl]-phenyl}-N-hydroxyacrylamide

or a pharmaceutically acceptable salt or prodrug thereof.

37. A compound according to claim 1 selected from the group consisting of

OH OH

6-(3-Benzoyl-ureido)-hexanoic acid hydroxyamide,

NH OH

8-(3-Benzoyl-ureido)-octanoic acid hydroxyamide,

4-(3-Benzoyl-ureidomethyl)-N-hydroxybenzamide,

NHOH NHOH

3-(4-{3-Benzoyl-1-[2-(1H-indol-3-yl)-ethyl]-ureidomethyl}-phenyl)-N-hydroxy-acrylamide,

HN O O N OH

3-[4-(3-Benzoyl-1-phenethyl-ureidomethyl)-phenyl]-N-hydroxy-acrylamide,

NH NH OH

6-(3-Benzoyl-thioureido)-hexanoic acid hydroxyamide,

3-{4-[3-Benzoyl-1-(2-piperidin-1-yl-ethyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

25

30

136

3-{4-[3-Benzoyl-1-(2-pyrrolidin-1-yl-ethyl)-ureidomethyl]-phenyl}-N-hydroxy-acrylamide,

or a pharmaceutically acceptable salt or prodrug thereof.

- 38. A pharmaceutical composition including a compound according to any one of claims 1 to 37 and a pharmaceutically acceptable diluent, excipient or carrier.
 - 39. Use of a compound according to any one of claims 1 to 37 in the preparation of a medicament for the treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation and/or angiogenesis.

40. A use according to claim 39 wherein the disorder is a proliferative disorder.

41. A use according to claim 40 wherein the proliferative disorder is cancer.

- 42. A use according to claim 41 wherein the cancer is selected from breast cancer, lung cancer, ovarian cancer, prostate cancer, head and neck cancer, renal cancer, gastric cancer, colon cancer, pancreatic cancer and brain cancer.
- 43. A method of treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation and/or angiogenesis in a patient the method including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 37 to the patient.
 - 44. A method according to claim 43 wherein the disorder is a proliferative disorder.
 - 45. A method according to claim 44 wherein the proliferative disorder is cancer.
 - 46. A method according to claim 45 wherein the cancer is selected from breast cancer, lung cancer, ovarian cancer, prostate cancer, head and neck cancer, renal cancer, gastric cancer, colon cancer, pancreatic cancer and brain cancer.

137

- 47. Use of a compound according to any one of claims 1 to 37 or a pharmaceutical composition according to claim 38 to modify deacetylase activity.
- 48. A use according to claim 47 wherein the deacetylase activity is histone deacetylase activity.
 - 49. A use according to claim 47 wherein the deacetylase activity is class I histone deacetylase activity.
- 10 50. A use according to claim 48 or 49 wherein the histone deacetylase is HDAC1.
 - 51. A use according to claim 48 or 49 wherein the histone deacetylase is HDAC8.
- 52. A method of modifying deacetylase activity including contacting the deacetylase with a compound according to any one of claims 1 to 37.
 - 53. A method according to claim 52 wherein the deacetylase activity is histone deacetylase activity.
- 20 54. A method according to claim 52 wherein the deacetylase activity is class I histone deacetylase activity.
 - 55. A method according to claim 53 or 54 wherein the histone deacetylase is HDAC1.
- 25 56. A method according to claim 53 or 54 wherein the histone deacetylase is HDAC8.
 - 57. A method of treatment of a disorder that can be treated by the inhibition of deacetylase activity in a patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 37 to the patient.
 - 58. A method according to claim 57 wherein the deacetylase activity is histone deacetylase activity.

30

59. A method of treatment of a disorder that is mediated by histone deacetylase activity in a patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 37 to the patient.

PCT/SG2004/000353

- 138 60. A method according to any one of claims 57 to 59 wherein the disorder is selected from the group consisting of Proliferative disorders (e.g. cancer); Neurodegenerative diseases including Huntington's Disease, Polyglutamine diseases, Parkinson's Disease, Alzheimer's Disease, Seizures, Striatonigral degeneration, Progressive supranuclear palsy, Torsion dystonia, Spasmodic torticollis and dyskinesis, Familial tremor, Gilles de la 5 Tourette syndrome, Diffuse Lewy body disease, Progressive supranuclear palsy, Pick's disease, Intracerebral haemorrhage, Primary lateral sclerosis, Spinal muscular atrophy, Amyotrophic lateral sclerosis, Hypertrophic interstitial polyneuropathy, Retinitis pigmentosa, Hereditary optic atrophy, Hereditary spastic paraplegia, Progressive ataxia 10 and Shy-Drager syndrome; Metabolic diseases including Type 2 diabetes; Degenerative Diseases of the Eye including Glaucoma, Age-related macular degeneration, Rubeotic glaucoma, Interstitial keratitis, Diabetic retinopathy; Inflammatory diseases and/or Immune system disorders including Rheumatoid Arthritis (RA), Osteoarthritis, Juvenile chronic arthritis, Graft versus Host disease, Psoriasis, Asthma, Spondyloarthropathy, 15 Crohn's Disease, Inflammatory bowel disease, Colitis Ulcerosa, Alcoholic hepatitis. Diabetes, Sjoegrens's syndrome, Multiple Sclerosis, Ankylosing spondylitis, Membranous glomerulopathy, Discogenic pain, Systemic Lupus Erythematosus; Disease involving angiogenesis including cancer, psoriasis, rheumatoid arthritis; Psychological disorders including bipolar disease, schizophrenia, mania, depression and dementia;
- 20 Cardiovascular Diseases including Heart failure, restenosis and arteriosclerosis; Fibrotic diseases including liver fibrosis, cystic fibrosis and angiofibroma; Infectious diseases including Fungal infections, such as Candida Albicans, Bacterial infections, Viral infections, such as Herpes Simplex, Protozoal infections, such as Malaria, Leishmania infection, Trypanosoma brucei infection, Toxoplasmosis and coccidiosis and
- 25 Haematopoletic disorders including thalassemia, anemia and sickle cell anemia.
 - 61. A method for inhibiting cell proliferation including administration of an effective amount of a compound according to any one of claims 1 to 37.
- 30 62. A method of treatment of a neurodegenerative disorder in a patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 37 to the patient.
- 63. A method according to claim 62 wherein the neurodegenerative disorder is Huntington's Disease.

139

- A method of treatment of an inflammatory disease and/or immune system disorder in a patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 37 to the patient.
- 5 65. A method according to claim 64 wherein the inflammatory disease and/or immune system disorder is rheumatoid arthritis.
 - 66. A method according to claim 64 wherein the inflammatory disease and/or immune system disorder is systemic lupus erythematosus.
 - 67. The use of a compound according to any one of claims 1 to 37 in the manufacture of a medicament for the treatment of cancer.
 - 68. A use according to claim 67 wherein the cancer is a hematologic malignancy.
- 15 69. A use according to claim 68 wherein the hematologic malignancies are selected from a group consisting of B-cell lymphoma, T-cell lymphoma and leukemia.
 - 70. A use according to claim 67 wherein the cancer is a solid tumor.

10

- 71. A use according to claim 70 wherein the solid tumor is selected from the group consisting of breast cancer, lung cancer, ovarian cancer, prostate cancer, head and neck cancer, renal cancer, gastric cancer, colon cancer, pancreatic cancer and brain cancer.
 - 72. A method of treatment of a proliferative disorder in patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 37 to the patient.
 - 73. A method of treatment of cancer in patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 37 to the patient.
- 30 74. A method according to claim 73 wherein the cancer is a hematologic malignancy.
 - 75. A method according to claim 74 wherein the hematologic malignancy is selected from the group consisting of B-cell lymphoma, T-cell lymphoma and leukemia.
 - 76. A method according to claim 73 wherein the cancer is a solid tumor.

- 77. A method according to claim 76 wherein the solid tumor is selected from the group consisting of breast cancer, lung cancer, ovarian cancer, prostate cancer, head and neck cancer, renal cancer, gastric cancer, colon cancer, pancreatic cancer and brain cancer.
- 5 78. Use of a compound according to any one of claims 1 to 37 in the manufacture of a medicament for the induction of apoptosis of tumor cells.
 - 79. A method of induction of apoptosis of a cell including contacting the cell with an effective amount of a compound according to any one of claims 1 to 37.